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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,265	12/10/2001	Yumio Kudo	1110-0305P	6012

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EXAMINER	
DI NOLA BARON, LILIANA	

ART UNIT	PAPER NUMBER
1615	11

DATE MAILED: 10/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,265	KUDO ET AL.	
	Examiner	Art Unit	
	Liliana Di Nola-Baron	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *August 12, 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of Applicant's amendment, filed on August 12, 2003, is acknowledged.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watanabe et al. (U.S. Patent 6,368,629) in view of Iida (EPO 0284039).

Watanabe et al. provides a system for releasing a drug in the colon, said system comprising a drug coated with an organic acid-soluble polymer material and a saccharide, and further coated with an enteric coating polymer (See col. 4, line 46 to col. 6, line 3). Watanabe et al. teaches that the saccharide is degraded by enterobacteria in the lower gastrointestinal tract and can be a polysaccharide (See col. 7, lines 26-34), and includes Eudragit E (dimethylaminoethyl methacrylate-methyl methacrylate-butyl methacrylate copolymer) and chitosan as specific examples of polymers used in the invention (See col. 9, lines 20-24). Watanabe et al. teaches that the polymer may contain a release-controlling material, such as Eudragit RS and ethyl cellulose (See col. 9, lines 24-50). Watanabe et al. teaches that the preparation may be in any dosage form, such as tablets, granules, powders and capsules (See col. 12, lines 4-6).

Thus, Watanabe et al. discloses formulations comprising a material degraded by enterobacteria, which can be a polysaccharide, polymer B, a substance that control disintegration and enteric coating, as claimed in the instant application. Watanabe et al. is deficient in the fact, that it does not include a compound having a disulfide bond in the formulations of the invention.

Iida discloses slow-release pharmaceutical compositions comprising a slow-release rendering additive, specifically cystine (See p. 2, line 52 to p. 3, line 3). Iida teaches that the composition can be used with any drug, the layer containing the active ingredient may be compressed with a layer containing no active ingredient, the mixed powder may be mixed with a binder, and enteric granules may be prepared by coating the first granulate with an enteric polymer (See p. 3, line 51 to p. 4, line 13). Additionally, Iida teaches that granules may be compressed into tablets, which may be coated with an enteric coating and provided with a sugar coating, or formed into capsules (See p. 4, lines 14-29).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the formulations disclosed by Watanabe et al., by including cystine as slow-release agent, to assure release of the drug in the lower gastrointestinal tract. The expected result would have been successful compositions and formulations for the controlled release of drugs in the colon or intestine. Because of the teachings of Iida, that formulations comprising a layer comprising cystine and an active ingredients can be combined with additional ingredients and further coated with enteric polymers, one of ordinary skill in the art would have a reasonable expectation that the compositions claimed in the instant application would be

successful. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

3. Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Plate` et al. (U.S. Patent 6,004,583).

Plate` et al. provides a composition comprising a water-swellable polymer, which is chemically modified with an agent that reduces degradation of drugs, and a drug and includes dimethylaminoalkyl methacrylate and chitosan among the polymers used in the invention (See col. 7, line 36 to col. 9, line 15). Plate` et al. includes additional swellable polymers as useful in the invention, such as agar, cellulose and pectin (See col. 11, lines 46-67). Plate` et al. teaches that the polymer must be modified with a material which contains a proteolitic inhibitor and a binding agent, specifically ovomucoid, and the thiol group of cystine from the protein inhibitor can be coupled to the polymer (See col. 17, line 20 to col. 18, line 28). Plate` et al. teaches that the compositions of the invention may be administered as tablets or capsules, which are enterically coated (See col. 20, lines 3-10).

The patent provides the general teachings that the formulations of the invention comprise the modified polymer and the drug, without specifying whether the drug is mixed or coated with the polymer of the invention. However, one of ordinary skill in the art would have been able to determine the best formulation by routine experimentation and clinical trials.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of Plate`et al. to device a system for drug delivery in

the lower gastrointestinal tract. The expected result would have been successful compositions and formulations for the controlled release of drugs in the colon or intestine. Because of the teachings of Plate` et al., that formulations comprising a swellable polymer modified to be coupled to cystine and an active ingredients can be combined with additional ingredients and further coated with enteric polymers, one of ordinary skill in the art would have a reasonable expectation that the compositions claimed in the instant application would be successful. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

4. Applicant's arguments filed on August 12, 2003 have been fully considered but they are not persuasive.

5. Applicant argues that the saccharide is an essential ingredient in the invention disclosed in Watanabe et al., whereas no saccharide is required in Applicant's claimed invention. In response to said argument, it is noted that the "comprising" language in the instant claims allows for the presence of additional ingredients in the compositions disclosed by the prior art.

6. In response to Applicant's argument, that Iida does not disclose or suggest a slow-release composition that releases the drug selectively in the lower gastrointestinal tract, it is noted that the examiner relies on Iida for the teachings that the presence of cystine in pharmaceutical compositions causes the slow release of the drug from the compositions, and said compositions may be in the form of tablets, granules or capsules and enteric coated. The examiner relies on

Watanabe et al. for the teachings of systems for the release of a drug specifically in the colon of the gastrointestinal tract.

7. Applicant argues that there is no motivation to chose cystine from the group of adenine, cystine and tyrosine disclosed by Iida. In response to said argument, it is noted that Iida clearly discloses and suggests cystine as slow release rendering additive (See p. 3, lines 1-3). Therefore one of ordinary skill in the art would have been led to the selection of cystine in view of the fair reading of the teachings found in Iida.

8. In response to Applicant's argument, that the slow release tablet containing cystine disclosed by Iida in Example 9 probably does not dissolve because the dissolution profile in solution is at pH 6.8, it is noted that Example 3 in Iida is directed to compositions comprising cystine wherein the dissolution profile in solution is at pH 1.2. Furthermore, the examples disclosed by the prior art are the inventor's best mode, and the examples do not need to show the specific combination claimed by Applicant.

9. In response to Applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the properties of the claimed composition at specific pH) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

10. In response to Applicant's argument that in Plate` et al. the cystine is not added for the value of the disulfide bond, the fact that Applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for

patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

11. In reply to Applicant's argument, that the compositions disclosed by Plate` et al. are not enteric, it is noted that Applicant's claimed invention is directed to compositions comprising ingredients, which are disclosed by the prior art, and Plate` et al. teaches that the compositions of the invention may be administered as tablets or capsules and are enterically coated for the delivery of drugs to the intestinal tract (See col. 20, lines 3-10).

12. In response to Applicant's argument, that Plate` et al. fails to disclose specific disintegration in the lower gastrointestinal tract, it is noted that the reference specifically teaches that the therapeutic composition passes into the intestinal tract without being significantly affected by or degradated in the stomach, and is disintegrated in the intestinal tract (See col. 20, lines 8-11).

13. In response to Applicant's argument, that Plate` et al. fails to disclose a composition of cystine and chitosan, it is noted that the reference includes chitosan among the polymers used in the invention (See col. 7, line 36 to col. 9, line 15) and teaches that the thiol group of cystine from the protein inhibitor can be coupled to the polymer (See col. 17, line 20 to col. 18, line 28). The chitosan disclosed by the prior art may be decomposed by enterobacteria.

Conclusion

14. Claims 1-14 stand rejected.

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318. The examiner can normally be reached on Monday through Thursday, 5:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.

LDNB

October 3, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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